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IMMUNOGLOBULIN VARIANTS

Relation back and Priority Information

This is a continuation of U.S. Ser. No. 08/466,163, filed on June 6, 1995, now allowed, which is a division of U.S. Ser. No. 08/405,617, filed on March 15, 1995, which is a continuation of U.S. Ser. No. 08/185,899, filed on January 26, 1994, now abandoned, which is a 35 U.S.C. § 371 of PCT/US92/06860, filed on August 14, 1992, which is a continuation-in-part of both U.S. Ser. No. 07/879,495, filed on May 7, 1992, now abandoned and U.S. Ser. No. 07/744,768, filed on August 14, 1991, now abandoned; all of which are incorporated by reference and to which application priority is claimed under 35 U.S.C. § 120.

Background of the Invention

This invention relates to amino acid sequence variant anti-IgE antibodies and to polypeptides containing IgE sequences, especially IgE antagonists and to polypeptides capable of differential binding to FcεRI and FcεRII.

IgE is a member of the immunoglobulin family that mediates allergic responses such as asthma, food allergies, type 1 hypersensitivity and the familiar sinus inflammation suffered on a widespread basis. IgE is secreted by, and expressed on the surface of, B-cells. IgE synthesized by B-cells is anchored in the B-cell membrane by a transmembrane domain linked to the mature IgE sequence by a short membrane binding region. IgE also is bound to B-cells (and monocytes, eosinophils and platelets) through its Fc region to a low affinity IgE receptor (FcεRII, hereafter "FCEL"). Upon exposure of a mammal to an allergen, B-cells are clonally amplified which synthesize IgE that binds the allergen. This IgE in turn is released into the circulation by the B-cells where it is bound by B-cells (through the FCEL) and by mast cells and basophils through the so-called high affinity receptor (FcεRI, hereinafter "FCEH") found on the surface of the mast cells and basophils. Such mast cells and basophils are thereby sensitized for allergen. The next exposure to the allergen cross-links the FcεRI on these cells and thus activates their release of histamine and other factors which are responsible for clinical hypersensitivity and anaphylaxis.

The art has reported antibodies capable of binding to FCEL-bound IgE but not IgE located on FCEH (see for example WO 89/00138 and ~~US patent~~ **U.S. Pat. No.** 4,940,782).